

choleraesuis, Salmonella dublin, Escherichia coli, Haemophilus influenzae, Neisseria gonorrhoeae, Yersinia enterocolitica, Bordetella pertussis or Brucella abortus.

39. (New) The method according to claim 20 wherein the bacterium is genetically engineered to express an antigen from another organism.

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40. (New) The method according to claim 39 wherein the antigen is fragment C of tetanus toxin.

41. (New) The method according to claim 39 wherein expression of the antigen is driven by the *nirB* promoter or the *htrA* promoter.

REMARKS

Reconsideration of the application and entry of the foregoing amendments are requested.

Claims 2 to 6, 21 to 24, 26, and 28 to 30 have been cancelled. Claims 31 to 41 have been added. Claims 1, 7 to 17, 20, 25, and 27 have been amended. Thus, claims 1, 7 to 17, 20, 25, 27, and 31 to 41 are pending in the application.

The main amendments are as follows:

1. Claim 6 has been combined with claim 1 to specify that the mutated gene is the *surA* gene.
2. Similarly, claim 20 has been amended to specify that the mutated gene is the *surA* gene.
3. Claim 1 has been amended to recite "A composition which invokes an immune response to a pathogenic bacterium . . ." rather than "A

vaccine” Claims 7 to 17, 25, and 27, which depend directly or indirectly on claim 1, have also been amended to recite “[t]he composition”

4. Claim 20 has been amended to refer to “invoking” an immune response instead of “raising” an immune response.
5. New claims 31 to 41 have been added. These claims are essentially the same as composition claims 7 to 17 except that they are in method format instead of composition format.

The amendments are being made solely to advance the application to allowance and do not constitute an acquiescence, abandonment, or disclaimer with respect to any subject matter originally claimed. Applicants reserve the right to pursue excluded subject matter by way of one or more continuing applications.

Rejections under 35 U.S.C. § 112, first paragraph

Reconsideration of the rejection of claims 1 to 17 and 20 to 30 for lack of an enabling disclosure is requested.

Applicants ask the Examiner to note that the claims no longer recite a mutation in any gene encoding a protein which promotes folding of extracytoplasmic proteins but rather recite a mutation specifically in the *surA* gene.

Applicants also ask the Examiner to note that the claims no longer recite a “vaccine,” but rather recite “A composition which invokes an immune response to a pathogenic bacterium” Thus, the claims now presented do not require that the composition induces protective immunity, but rather merely require an ability to invoke an immune response.

It is common general knowledge that the immune system is able to respond to essentially any non-self organism. The environment contains thousands of

different pathogens, and it is one of the fundamental tenets of immunity that the immune system is able to respond to essentially any pathogen with which it is presented. There can therefore be no doubt that the attenuated pathogenic bacteria recited in the claims do invoke an immune response.

Reconsideration of the rejection of claims 1 to 17 and 20 to 30 for lack of written description is also requested. For reasons analogous to those given above in connection with the rejection for lack of enabling disclosure, there can be no doubt that Applicants had possession of bacteria that are able to invoke an immune response and that the specification describes such bacteria. Essentially any bacterium is able to invoke an immune response.

Rejections under 35 U.S.C. § 112, second paragraph

As regards the rejection made in paragraph 5 of the Office Action, the relevant dependent claims now recite “The” composition as opposed to “A” composition.

In paragraph 6 of the Office Action, the Examiner argued that it is unclear how to define “raising” an immune response and whether “raising” is equivalent to “invoking.” Claim 20 now refers to “invoking” an immune response.

As regards items 7, 8, and 9 of the Office Action, the rejected claims, claims 28, 29, and 30, have been cancelled.

Rejection under 35 U.S.C. § 102

Reconsideration of the rejection over Lazar *et al.* is requested. The amended claims specify that the bacterium is a “pathogenic” bacterium attenuated by a mutation in the *surA* gene. This clearly distinguishes the claims over Lazar *et al.* because Lazar *et al.* describes the use of non-pathogenic, laboratory strains of *E. coli*. Lazar *et al.* does not in fact have anything at all to do with invoking an

Amendment and Response
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immune response against pathogenic bacteria, but rather describes experiments to investigate the biochemical function that SurA plays in the cell.

It is respectfully submitted that the application is in condition for allowance, and a notice to that effect is requested.

Applicants respectfully request that the Examiner acknowledge receipt of the claim for Foreign Priority Under 35 U.S.C. § 119 and the certified copy of the U.K. priority document that were filed on May 3, 2001.

If any additional fees are due in connection with the filing of this paper, please charge the fees to our Deposit Account No. 16-2312. If a fee is required for an extension of time under 37 C.F.R. § 1.136 not accounted for above, such an extension is requested and the fee should also be charged to our deposit account.

Respectfully submitted,

Dated: February 19, 2003

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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants: Steven Neville Chatfield et al. Attorney Docket: KCO1003US
Serial No.: 09/591,447 Group Art Unit: 1645
Filed: June 9, 2000 Examiner: Ja-Na Hines
For: VACCINES CONTAINING ATTENUATED BACTERIA

MARKED-UP VERSION OF PRIOR PENDING CLAIMS

1. (Amended) A [vaccine] composition which invokes an immune response to a pathogenic bacterium comprising [a pharmaceutically acceptable carrier or diluent and] a pathogenic bacterium attenuated by a non-reverting mutation in [a gene encoding a protein which promotes folding of extracytoplasmic proteins] the *surA* gene and a pharmaceutically acceptable carrier or diluent.

7. (Twice amended) The composition [A vaccine] according to claim 1 wherein the bacterium is further attenuated by a non-reverting mutation in a second gene.

8. (Amended) The composition [A vaccine] according to claim 7 wherein the second gene is an *aro* gene, a *pur* gene, the *htrA* gene, the *ompR* gene, the *galE* gene, the *cya* gene, the *crp* gene or the *phoP* gene.

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Date: February 19, 2003

Signature:

Name: Jodi Jung

9. (Amended) The composition [A vaccine] according to claim 8 wherein the *aro* gene is *aroA*, *aroC*, *aroD* or *aroE*.
10. (Twice amended) The composition [A vaccine] according to claim 1 wherein the mutation in the *surA* gene [encoding a protein which promotes folding of extracytoplasmic proteins] is a defined mutation.
11. (Twice amended) The composition [A vaccine] according to claim 1 wherein the bacterium has no uncharacterised mutations in the genome thereof.
12. (Twice amended) The composition [A vaccine] according to claim 1 wherein the bacterium is a bacterium that infects via the oral route.
13. (Twice amended) The composition [A vaccine] according to claim 1 wherein the bacterium is from the genera *Salmonella*, *Escherichia*, *Vibrio*, *Haemophilus*, *Neisseria*, *Yersinia*, *Bordetella* or *Brucella* [*Salmonella*, *Escherichia*, *Vibrio*, *Haemophilus*, *Neisseria*, *Yersinia*, *Bordetella* or *Brucella*].
14. (Amended) The composition [A vaccine] according to claim 13 wherein the bacterium is *Salmonella typhimurium*, *Salmonella typhi*, *Salmonella enteritidis*, *Salmonella choleraesuis*, *Salmonella dublin*, *Escherichia coli*, *Haemophilus influenzae*, *Neisseria gonorrhoeae*, *Yersinia enterocolitica*, *Bordetella pertussis* or *Brucella abortus*.
15. (Twice amended) The composition [A vaccine] according to claim 1 wherein the bacterium is genetically engineered to express an antigen from another organism.

16. (Amended) The composition [A vaccine] according to claim 15 wherein the antigen is fragment C of tetanus toxin.

17. (Twice amended) The composition [A vaccine] according to claim 15 wherein expression of the antigen is driven by the *nirB* promoter or the *htrA* promoter.

20. (Amended) A method of [raising] invoking an immune response in a host to a pathogenic bacterium, which method comprises administering to the host a pathogenic bacterium attenuated by a non-reverting mutation in [a gene encoding a protein which promotes folding of extracytoplasmic proteins] the *surA* gene.

25. (Amended) The composition [A vaccine] according to claim 7 wherein the mutation in the second gene is a defined mutation.

27. (Amended) The composition [A vaccine] according to claim 16 wherein expression of the antigen is driven by the *nirB* promoter or the *htrA* promoter.